ENRECO, Inc.

'99 NOV 23 A9:44

November 22, 1999

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

RE: For Inclusion in your Docket #91N-0103

To Whom It May Concern:

It seems unlikely that the FDA would miss important papers in the medical literature-but there are four 1999 papers about two large studies that clearly document cardiovascular health benefits of balancing the essential fatty acids in foods (increasing omega-3 and decreasing omega-6). They are:

1. The Final Report of the Lyon Diet Heart Study by Michael deLogeril et al, Circulation 99: 779-785, 1999
2. An Editorial on the Lyon Diet Heart Study by A. Leaf, Circulation 99: 733735, 1999
3. The results of the GISSI-Prevenzione trial by the large group of investigators in Lancet **354:**
   447-455, 1999
4. An editorial comment on the GISSI results by Morris Brown in Lancet 354: 44 l-442, 1999

The results in these reports provide clear support for the claim of cardiovascular benefits of including omega-3 fats in the daily diet and encourage reversal of the earlier FDA denial of the claim.

In addition, results from the US Physicians Health Study reported that consumption of fish at least once per week may reduce the risk of sudden cardiac death in men (CM Albert et al, J.Am.Med. Assoc. 279:23-28, 1998), and it was discussed by NF Sheard in Nutrition Reviews 56: 177-179, 1998.

In 1999, the many reports of omega-3 fats diminishing high blood pressure in animals were extended to humans by TA Mori et al, in Hypertension 34: 253-260, 1999, who demonstrated reduction of ambulatory blood pressure and heart rate.

91N-0103

Making the best foods better!

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As for significant scientific agreement, an expert workshop convened in Europe concluded that omega-3 fatty acids are protective agents that may reduce the risk of coronary heart disease (EAM deDeckere et al, European J. Clin. Nutr. 52:749-753,1998).

A similar conclusion was produced from an expert workshop held at the NIH in Bethesda in April 1999 and from a separate expert workshop convened at the University of Maryland in Baltimore in June, 1999.

Enclosed please find 60 citations downloaded from the National Library of Medicine on studies done on the positive benefits of increasing omega-3 fatty acids in the diet. Also included are selected full citations specifically related to omega-3 fatty acids and heart disease.

I think that the power of these recent studies plus all of the work done since 1973 by Dr. William Lands, Senior Scientific Advisor, NIAAA, proves beyond a shadow of a doubt that Omega-3 is beneficial for preventing and treating heart disease, especially when it comes to weighing the low effectiveness of drug treatments and considerable side-effects. Besides, a mountain of evidence shows other beneficial effects of Omega-3 on mental heaith, immune system, bone metabolism, and the functioning of the retina. For references for these statements, you may check over 2500 references available at www.flax.com.

If the FDA wants to show that they respect the scientific *community* more than the political community, they will certainly support the idea that Omega-3 is beneficial in preventing and treating cardiovascular disease.

Sincerely,

Paul A Stitt, MS CNS
President
ENRECO, INC.

PAS:bmk

Enclosures: As listed above
Copy of this letter and enclosures

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Citations 1 to 20 of 61 from MEDLINE

r TITLE: **Serotonin fails to induce proliferation of endotbelial cells preloaded with eicosapentaenoic acid and docosahexaenoic acid.**
Full Citation
AUTHORS: **Pakala R, et al.**
SOURCE: **Atherosclerosis. 1999 Jul;145(1): 137-46.**
Related Articles CIT. IDS: **PMID: 10428304 UI: 99355258**

r TITLE: **Equal antithrombotic and triglyceride-lowering effectiveness of eicosapentaenoic acid-rich and docosahexaenoic acid-rich fish oil supplements.**
Full Citation
AUTHORS: **Howe PR, et al.**
SOURCE: **Lipids. 1999;34 Suppl:S307-8. No abstract available.**
Related Articles CIT. IDS: **PMID: 10419186 UI: 99345554**

r TITLE; **n-3 fatty acids and human lipoprotein metabolism: an update.**
Full Citation
AUTHORS: **Harris WS**
SOURCE: **Lipids. 1999;34 Suppl:S257-8. No abstract available.**
Related Articles CIT. IDS: **PMID: 10419172 UI: 99345540**

r TITLE: **Docosahexaenoic acid is an antihypertensive nutrient that affects aldosterone production in SHR**
Full Citation
AUTHORS: **Engler MM, et al.**
SOURCE: **Proc Soc Exp Biol Med. 1999 May;221(1):32-8.**
Related Articles CIT. IDS: **PMID: 10320629 UI: 99255846**

r TITLE: **Prevention of sudden cardiac death by dietary pure omega-3 polyunsaturated fatty acids in dogs.**
Full Citation
AUTHORS: **Billman GE, et al.**
SOURCE: **Circulation. 1999 May 11;99(18):2452-7.**
Related Articles CIT. IDS: **PMID: 10318669 UI: 99252130**

r TITLE: Concentration of serum lipids and aortic lesion size in female and male apo E-deficient mice fed docosahexaenoic acid.

Full Citation AUTHORS: Adan Y, et al.

SOURCE: Biosci Biotechnol Biochem. 1999 Feb;63(2):309-13.

Related Articles CIT. IDS: PMID: 10192911 UI: 99208991

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r TITLE: Effects of docosahexaenoic and eicosapentaenoic acid on lipid metabolism, eicosanoid production, platelet aggregation and atherosclerosis in bypercholesterolemic rats.

Full Citation AUTHORS: Adan Y, et al.

SOURCE: Biosci Biotechnol Biochem. 1999 Jan;63(1):111-9.

Related Articles CIT. IDS: PMID: 10052130 UI: 99161282

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r TITLE: Individual effects of dietary EPA and DHA on the functioning of the isolated working rat heart.

Full Citation AUTHORS: Sergiel JP, et al.

SOURCE: Can J Physiol Pharmacol. 1998 Jul-Aug;76(7-8):728-36.

Related Articles CIT. IDS: PMID: 10030453 UI: 99153524

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r TITLE: Effect of docosahexaenoic acid on intracellular calcium dynamics in vascular smooth muscle cells from normotensive and genetically hypertensive rats.

Full Citation AUTHORS: Hirafuji M, et al.

SOURCE: Res Commun Mol Pathol Pharmacol. 1998 Oct;102(1):29-42.

Related Articles CIT. IDS: PMID: 9920344 UI: 99117072

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r TITLE: Effect of medium-term supplementation with a moderate dose of n-3 polyunsaturated fatty acids on blood pressure in mild hypertensive patients.

Full Citation AUTHORS: Prisco D, et al.

SOURCE: Thromb Res. 1998 Aug 1;91(3):105-12.

Related Articles CIT. IDS: PMID: 9733153 UI: 98401989

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r TITLE: Docosahexaenoic acid inhibits blood viscosity in stroke-prone spontaneously hypertensive rats.

Full Citation AUTHORS: Kimura S, et al.

SOURCE: Res Commun Mol Pathol Pharmacol. 1998 Jun;100(3):351-61.

Related Articles CIT. IDS: PMID: 9730013 UI: 98397742

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r TITLE: Docosahexaenoic acid-enriched milk.
Full Citation AUTHORS: Wright T, et al.
SOURCE: World Rev Nutr Diet. 1998;83: 160-5. Review. No abstract available.
Related Articles CIT. IDS: PMID: 9648512 UI: 98312318

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r TITLE: Ameliorative effects of docosahexaenoic acid on serum lipid changes in stroke-prone spontaneously hypertensive rats.
Full Citation AUTHORS: Kimura S, et al.
SOURCE: Res Commun Mol Pathol Pharmacol. 1998 Apr;100(1):53-64.
Related Articles CIT.IDS: PMID: 9644719 UI: 98308589

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r TITLE: Intraamniotic ethyl docosahexaenoate administration protects fetal rat brain from ischemic stress.
Full Citation AUTHORS: Glozman S, et al.
SOURCE: J Neurochem. 1998 Jun;70(6):2484-91.
Related Articles CIT. IDS: PMID: 9603213 UI: 98264352

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r TITLE: The effects of purified eicosapentaenoic and docosahexaenoic acids on arterial thrombosis tendency and platelet function in rats.
Full Citation AUTHORS: Nieuwenhuys CM, et al.
SOURCE: Biochim Biophys Acta. 1998 Feb 23; 1390(3):313-22.
Related Articles CIT. IDS: PMID: 9487152 UI: 98155201

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r TITLE: Is a dietary n-3 fatty acid supplement able to influence the cardiac effect of the psychological stress?
Full Citation AUTHORS: Rousseau D, et al.
SOURCE: Mol Cell Biochem. 1998 Jan;178(1-2):353-66.
Related Articles CIT. IDS: PMID: 9546620 UI: 98206697

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r TITLE: Effect of supplementation with different doses of DHA on the levels of circulating DHA as non-esterified fatty acid in subjects of Asian Indian background.
Full Citation AUTHORS: Conquer JA, et al.
SOURCE: J Lipid Res. 1998 Feb;39(2):286-92.
Related Articles CIT. IDS: PMID: 9507989 UI: 98167407

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r TITLE: [Specific modulation of vascular smooth muscle cell functions by docosahexaenoic acid].

Full Citation AUTHORS: Hirafuji M, et al.

SOURCE: Nippon Yakurigaku Zasshi. 1997 Oct; 110 Suppl 1: 171P-176P. Japanese.

Related Articles CIT. IDS: PMID: 9503427 UI: 98164168

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r TITLE: Dietary docosahexaenoic acid increases cerebral acetylcholine levels and improves passive avoidance performance in stroke-prone spontaneously hypertensive rats.

{Full Citation AUTHORS: Minami M, et al.

SOURCE: Pharmacol Biochem Behav. 1997 Dec;58(4):1123-9.

Related Articles CIT. IDS: PMID: 9408223 UI: 98070161

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r TITLE: Are deficits of arachidonic and docosahexaenoic acids responsible for the neural and vascular complications of preterm babies?

Full Citation AUTHORS: Crawford MA, et al.

SOURCE: Am J Clin Nutr. 1997 Oct;66(4 Suppl):1032S-1041S. Review.

Related Articles CIT. IDS: PMID: 9322584 UI: 97463883

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Citations 21 to 40 of 61 from MEDLINE

r **TITLE:** Randomized, double-blind, placebo-controlled trial of fish oil and mustard oil in patients with suspected acute myocardial infarction: the Indian experiment of infarct survival--4.

Full Citation **AUTHORS:** Singh RR, et al.

SOURCE: Cardiovasc Drugs Ther. 1997 Jul;11(3):485-91.

Related Articles **CIT. IDS:** PMID: 9310278 UI: 97454203

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r **TITLE:** Effects of dietary docosahexaenoic acid on survival time and stroke-related behavior in stroke-prone spontaneously hypertensive rats.

Full Citation **AUTHORS:** Minami M, et al.

SOURCE: Gen Pharmacol. 1997 Sep;29(3):401-7.

Related Articles **CIT. IDS:** PMID: 9378247 UI: 98020726

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r **TITLE:** Suppressive action of docosahexaenoic acid enriched-Euglena on reduction of endothelium-dependent relaxation in stroke-prone spontaneously hypertensive rats (SHRSP).

Full Citation **AUTHORS:** Murakami T, et al.

SOURCE: J Nutr Sci Vitaminol (Tokyo). 1997 Apr;43(2):211-23.

Related Articles **CIT. IDS:** PMID: 9219094 UI: 97362630

☐ **TITLE:** [Effects of eifitol on lipid metabolism in patients with clinically different ischemic heart diseases].

Full Citation **AUTHORS:** Panchenko VM, et al.

SOURCE: Klin Med (Mosk). 1997;75(3):39-41. Russian. No abstract available.

Related Articles **CIT. IDS:** PMID: 9229613 UI: 97314590

☐ **TITLE:** Supplementation with an algae source of docosahexaenoic acid increases (n-3) fatty acid status and alters selected risk factors for heart disease in vegetarian subjects.

Full Citation **AUTHORS: Conquer JA, et al.**

SOURCE: J Nutr. 1996 Dec;126(12):3032-9.

Related Articles **CIT. IDS: PMID: 9001371 UI: 97154653**

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r **TITLE: The effects of omega-3 polyunsaturated (correction of polyunsatulated) fatty acids on the recovery of cardiac function following cold preservation and reperfusion in hyperlipidemic rats.**

Full Citation **AUTHORS: Ku K, et al.**

SOURCE: Transplantation. 1996 Sep 27;62(6):735-42.

Related Articles **CIT. IDS: PMID: 8824469 UI: 96421852**

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r **TITLE: Effects of eicosapentaenoic acid and docosahexaenoic acid diet supplement on tolerance to the cardiotoxicity of epirubicin and to ischaemia reperfusion in the isolated rat heart.**

Full Citation **AUTHORS: Schjott J, et al.**

SOURCE: Pharmacol Toxicol. 1996 Aug;79(2):65-72.

Related Articles **CIT. IDS: PMID: 8878248 UI: 97032352**

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r **TITLE: Exposure to the n-3 polyunsaturated fatty acid docosahexaenoic acid impairs alpha 1-adrenoceptor-mediated contractile responses and inositol phosphate formation in rat cardiomyocytes.**

Full Citation **AUTHORS: Reithmann C, et al.**

SOURCE: Naunyn Schmiedebergs Arch Pharmacol. 1996 Jul;354(2):109-19.

Related Articles **CIT. IDS: PMID: 8857587 UI: 97010549**

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r **TITLE: The cardiovascular protective role of docosahexaenoic acid.**

Full Citation **AUTHORS: McLennan P, et al.**

SOURCE: Eur J Pharmacol. 1996 Apr 4;300(1-2):83-9.

Related Articles **CIT. IDS: PMID: 8741170 UI: 96302989**

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r **TITLE: Effect of fish oil on heart rate variability in survivors of myocardial infarction: a double blind randomised controlled trial.**

Full Citation **AUTHORS: Christensen JH, et al.**

SOURCE: BMJ. 1996 Mar 16;312(7032):677-8. No abstract available.

Related Articles **CIT. IDS: PMID: 8597736 UI: 96182711**

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r TITLE: The chronic administration of docosahexaenoic acid reduces the spatial cognitive deficit following transient forebrain ischemia in rats.

Full Citation AUTHORS: Okada M, et al.

SOURCE: Neuroscience. 1996 Mar;71(1):17-25.

Related Articles CIT. IDS: PMID: 8834389 UI: 96431307

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r TITLE: [Effect of docanol on the status of hemostasis and fibrinolysis systems, as well as lipid spectrum in patients with ischemic heart disease depending on the initial level of fibrinolytic activity].

Full Citation AUTHORS: Liutova LV, et al.

SOURCE: Vopr Med Khim. 1996 Jan-Mar;42(1):64-70. Russian.

Related Articles CIT. IDS: PMID: 8999661 UI: 96377645

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r TITLE: Effects of n-3 polyunsaturated fatty acids on glucose homeostasis and blood pressure in essential hypertension. A randomized, controlled trial.

Full Citation AUTHORS: Toft I, et al.

SOURCE: Ann Intern Med. 1995 Dec 15;123(12):911-8.

/Related Articles CIT. IDS: PMID: 7486485 UI: 96072646

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r TITLE: Dietary docosahexaenoic acid (22:6n-3) prevents the development of hypertension in SHRSP.

Full Citation AUTHORS: Kimura S, et al.

SOURCE: Clin Exp Pharmacol Physiol. 1995 Dec;22 Suppl 1:S308-9.

Related Articles CIT. IDS: PMID: 8785821 UI: 96240820

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r TITLE: Effect of dietary docosahexaenoic acid in the rat middle cerebral artery thrombosis model.

Full Citation AUTHORS: Umemura K, et al.

SOURCE: Thromb Res. 1995 Jun 1;78(5):379-87.

Related Articles CIT. IDS: PMID: 7660354 UI: 95389405

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r TITLE: Dietary docosahexaenoic acid (22: 6n-3) prevents the development of hypertension in SHRSP.

Full Citation AUTHORS: Kimura S, et al.

SOURCE: Clin Exp Pharmacol Physiol Suppl. 1995;1:S308-9.

Related Articles CIT. IDS: PMID: 9072405 UI: 97076852

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r TITLE: **Increased proportion of docosahexanoic acid and high lipid peroxidation capacity in erythrocytes of stroke patients.**

Full Citation **AUTHORS: Imre SG, et al.**

SOURCE: Stroke. 1994 Dec;25(12):2416-20.

Related Articles **CIT. IDS: PMID: 7974583 UI: 95064908**

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r TITLE: **The omega-3 fatty acid docosahexaenoate reduces cytokine-induced expression of proatherogenic and proinflammatory proteins in human endothelial cells.**

Full Citation **AUTHORS: De Caterina R, et al.**

SOURCE: Arterioscler Thromb. 1994 Nov; 14(11): 1829-36.

Related Articles **CIT. IDS: PMID: 7524649 UI: 95034622**

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r TITLE: **The effects of n-3 fatty acid supplementation on bleeding time, plasma fatty acid composition, and in vitro platelet aggregation in cats.**

Full Citation **AUTHORS: Bright JM, et al.**

SOURCE: J Vet Intern Med. 1994 Jul-Aug;8(4):247-52.

Related Articles **CIT. IDS: PMID: 7983618 UI: 95074767**

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r TITLE: **Prevention of ischemia-induced ventricular fibrillation by omega 3 fatty acids.**

Full Citation **AUTHORS: Billman GE, et al.**

SOURCE: Proc Natl Acad Sci U S A. 1994 May 10;91(10):4427-30.

Related Articles **CIT. IDS: PMID: 8183925 UI: 94240150**

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Citations 4 1 to 60 of 6 1 from MEDLINE

r	TITLE:	**The relationship between the essential fatty acid status of mother and child and the occurrence of pregnancy-induced hypertension. Intermediate results of a prospective longitudinal study.**
Full Citation	AUTHORS:	**Al MD, et al.**
	SOURCE:	**World Rev Nutr Diet. 1994;76:110-3. No abstract available.**
Related Articles	CIT. IDS:	**PMID: 7856218 UI: 95159569**
r	TITLE:	**Infusion of EPA and DHA lipid emulsions: effects on heart lipids and tolerance to ischaemia-reperfusion in the isolated rat heart.**
Full Citation	AUTHORS:	**Schjott J, et al.**
	SOURCE:	**Scand J Clin Lab Invest. 1993 Dec;53(8):873-82.**
Related Articles	CIT. IDS:	**PMID: 8140399 UI: 94188692**
r	TITLE:	**[The effect of highly unsaturated fatty acids on the parameters of lipoprotein metabolism and rheology during their administration to patients undergoing chronic hemodialysis treatment].**
Full Citation	AUTHORS:	**Schmitt Y, et al.**
	SOURCE:	**Z Ernahrungswiss. 1993 Sep;32(3):209-18. German.**
Related Articles	CIT. IDS:	**PMID: 8237080 UI: 94055361**
⌐	TITLE:	**The influence of docosahexaenoic acid loading on stroke-prone spontaneously hypertensive rats.**
Full Citation	AUTHORS:	**Yasugi T, et al.**
	SOURCE:	**Ann N Y Acad Sci. 1993 Mar 15;676:70-82. No abstract available.**
Related Articles	CIT. IDS:	**PMID: 8489157 UI: 93256436**
r	TITLE:	**Effects of fish oil, nifedipine and their combination on blood pressure and lipids in primary hypertension.**
Full Citation	AUTHORS:	**Landmark K, et al.**

SOURCE: J Hum Hypertens. 1993 Feb;7(1):25-32.

Related Articles CIT. IDS: PMID: 8450517 UI: 93195904

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r TITLE: Can supplementation of diet with omega-3 polyunsaturated fatty acids reduce coronary angioplasty restenosis rate?

Full Citation AUTHORS: Bellamy CM, et al.

SOURCE: Eur Heart J. 1992 Dec;13(12):1626-31.

Related Articles CIT. IDS: PMID: 1289091 UI: 93170335

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r TITLE: The cumulative dose response effect of eicosapentaenoic and docosahexaenoic acid on blood pressure, plasma lipid profile and diet pattern in mild to moderate essential hypertensive black patients.

Full Citation AUTHORS: Du Plooy WJ, et al.

SOURCE: Prostaglandins Leukot Essent Fatty Acids. 1992 Aug;46(4):315-21.

Related Articles CIT. IDS: PMID: 1409770 UI: 93028637

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r TITLE: Effects of a combination of evening primrose oil (gamma linolenic acid) and fish oil (eicosapentaenoic + docahexaenoic acid) versus magnesium, and versus placebo in preventing pre-eclampsia.

Full Citation AUTHORS: D'Almeida A, et al.

SOURCE: Women Health. 1992;19(2-3):117-31.

Related Articles CIT. IDS: PMID: 1492408 UI: 93150614

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r TITLE: Plasmatic factors of haemostasis remain essentially unchanged except for PA1 activity during n-3 fatty acid intake in type I diabetes mellitus.

Full Citation AUTHORS: Spannagl M, et al.

SOURCE: Blood Coagul Fibrinolysis. 1991 Apr;2(2):259-65.

Related Articles CIT. IDS: PMID: 1832569 UI: 91370612

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r TITLE: Influence of fish oil on blood lipids in coronary artery disease.

Full Citation AUTHORS: Nikkila M

SOURCE: Eur J Clin Nutr. 1991 Apr;45(4):209-13.

Related Articles CIT. IDS: PMID: 1831755 UI: 91347985

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r TITLE: Suppression of atherogenesis by n-3 fatty acids in the cholesterol-fed rabbit.

Full Citation **AUTHORS: Demirogiu C, et al.**

SOURCE: Angiology. 1991 Apr;42(4):323-30.

Related Articles **CIT. IDS: PMID: 1826589 UI: 91196933**

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r **TITLE: [The role of n-3 polyunsaturated fatty acid on coronary heart disease].**

Full Citation **AUTHORS: Lu G**

SOURCE: Chung Hua Hsin Hsueh Kuan Ping Tsa Chih. 1990 Oct;18 (5):279-81. Chinese. No abstract available.

Related Articles **CIT. IDS: PMID: 2150806 UI: 91199916**

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r **TITLE: Effect of eicosapentaenoic and docosahexaenoic acids on blood pressure in hypertension. A population-based intervention trial from the Tromso study.**

Full Citation **AUTHORS: Bonaa KH, et al.**

SOURCE: N Engl J Med. 1990 Mar 22;322(12):795-801.

Related Articles **CIT. IDS: PMID: 2137901 UI: 90174237**

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r **TITLE: Fish oil: a panacea?**

Full Citation **AUTHORS: Bilo HJ, et al.**

SOURCE: Biomed Pharmacother. 1990;44(3):169-74. Review.

Related Articles **CIT. IDS: PMID: 2144459 UI: 90373932**

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r **TITLE: Effect of fish oil on blood pressure and serum lipids in hypertension and hyperlipidaemia.**

Full Citation **AUTHORS: Steiner A, et al.**

SOURCE: J Hypertens Suppl. 1989 May;7(3):S73-6.

Related Articles **CIT. IDS: PMID: 2547916 UI: 89341958**

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r **TITLE: Fish-oil dietary supplementation in patients with Raynaud's phenomenon: a double-blind, controlled, prospective study.**

Full Citation **AUTHORS: DiGiacomo RA, et al.**

SOURCE: Am J Med. 1989 Feb;86(2):158-64.

Related Articles **CIT. IDS: PMID: 2536517 UI: 89116243**

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r **TITLE: Short-term effects of omega-3 fatty acids on exercise stress test parameters, angina and lipoproteins.**

Full Citation **AUTHORS: Vacek JL, et al.**

SOURCE: Biomed Pharmacother. 1989;43(5):375-9. Review.

Related Articles CIT. IDS: PMID: 2551411 UI: 90001467

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r TITLE: Eskimo plasma constituents, dihomo-gamma-linolenic acid, eicosapentaenoic acid and docosahexaenoic acid inhibit the release of atherogenic mitogens.

Full Citation AUTHORS: Smith DL, et al.

SOURCE: Lipids. 1989 Jan;24(1):70-5.

Related Articles CIT. IDS: PMID: 2545997 UI: 89313134

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r TITLE: Eicosapentaenoic acid and adult diseases in Japan: epidemiological and clinical aspects.

Full Citation AUTHORS: Hirai A, et al.

SOURCE: J Intern Med Suppl. 1989;225(731):69-75.

Related Articles CIT. IDS: PMID: 2539836 UI: 89207014

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r TITLE: n-3 fatty acids as precursors for active metabolic substances: dissonance between expected and observed events.

Full Citation AUTHORS: Lands WE

SOURCE: J Intern Med Suppl. 1989;225(731):11-20. Review.

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TITLE:	**Fish consumption and risk of sudden cardiac death [see comments]**
AUTHORS:	**Albert CM; Hennekens CH; O'Donnell CJ; Ajani UA; Carey VJ; Willett WC; Ruskin JN; Manson JE**
AUTHOR AFFILIATION:	**Department of Medicine, Brigham and Women's Hospital, Boston, MA 02215- 1204, USA.**
SOURCE:	**JAMA 1998 Jan 7;279(1):23-8**
CITATION IDS:	**PMID: 9424039 UI: 98084655**
COMMENT:	**Comment in: JAMA 1998 Jan 7;279(1):65-6**
ABSTRACT:	**CONTEXT: Dietary fish intake has been associated with a reduced risk of fatal cardiac end points, but not with nonfatal end points. Dietary fish intake may have a selective benefit on fatal arrhythmias and therefore sudden cardiac death. OBJECTIVE: To investigate prospectively the association between fish consumption and the risk of sudden cardiac death. DESIGN: Prospective cohort study. SETTING: The US Physicians' Health Study. PATIENTS: A total of 20 551 US male physicians 40 to 84 years of age and free of myocardial infarction, cerebrovascular disease, and cancer at baseline who completed an abbreviated, semiquantitative food frequency questionnaire on fish consumption and were then followed up to 11 years. MAIN OUTCOME MEASURE: Incidence of sudden cardiac death (death within 1 hour of symptom onset) as ascertained by hospital records and reports of next of kin. RESULTS: There were 133 sudden deaths over the course of the study. After controlling for age, randomized aspirin and beta carotene assignment, and coronary risk factors, dietary fish intake was associated with a reduced risk of sudden death, with an apparent threshold effect at a consumption level of 1 fish meal per week (P for trend=.03). For men who consumed fish at least once per week, the multivariate relative risk of sudden death was 0.48 (95% confidence interval, 0.24-0.96; P=.04) compared with men who consumed fish less than monthly. Estimated dietary n-3 fatty acid intake from seafood also was associated with a reduced risk of sudden death but without a significant trend across increasing categories of intake. Neither dietary fish consumption nor n- 3 fatty acid intake was associated with a reduced risk of total myocardial infarction, nonsudden cardiac death, or total cardiovascular mortality. However, fish consumption was associated with a significantly reduced risk of**

	total mortality. CONCLUSION: These prospective data suggest that consumption of fish at least once per week may reduce the risk of sudden cardiac death in men.
MAIN MESH HEADINGS:	**Death, Sudden, Cardiac/*epidemiology** ***Seafood**
ADDITIONAL MESH HEADINGS:	**Adult** **Aged** **Aged, SO and over** **Cohort Studies** **Diet** **Fatty Acids, Omega-3** **Health Surveys** **Human** **Incidence** **Male** **Middle Age** **Multivariate Analysis** **Proportional Hazards Models** **Prospective Studies** **Risk** **Support, U.S. Gov't, P.H.S.** **United States/epidemiology**
PUBLICATION TYPES:	**JOURNAL ARTICLE**
CAS REGISTRY NUMBERS:	**0 (Fatty Acids, Omega-3)**
LANGUAGES:	**Eng**
GRANT/CONTRACT ID:	**CA-34944/CA/NCI** **CA-40360/CA/NCI** **HL-26490/HL/NHLBI** +

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TITLE:	**Fish consumption and the 30-year risk of fatal myocardial infarction [see comments]**
AUTHORS:	**Daviglus ML; Stamler J; Orencia AJ; Dyer AR; Liu K; Greenland P; Walsh MK; Morris D; Shekelle RB**
AUTHOR AFFILIATION:	**Department of Preventive Medicine, Northwestern University Medical School, Chicago, IL 60611, USA.**
SOURCE:	**N Engl J Med 1997 Apr 10;336(15):1046-53**
CITATION IDS:	**PMID: 9091800 UI: 97224090**
COMMENT:	**Comment in: N Engl J Med 1997 Aug 14;337(7):497-8; discussion 498-9** **Comment in: N Engl J Med 1997 Aug 14;337(7):498; discussion 498-9** **Comment in: N Engl J Med 1997 Aug 14;337(7);498-9** **Comment in: ACP J Club 1997 Nov-Dec;127(3):80**

ABSTRACT: **BACKGROUND: Epidemiologic data on the possible benefit of eating fish to reduce the risk of coronary heart disease have been inconsistent. We used data from the Chicago Western Electric Study to examine the relation between base-line fish consumption and the 30-year risk of death from coronary heart disease. METHODS: The study participants were 1822 men who were 40 to 55 years old and free of cardiovascular disease at base line. Fish consumption, as determined from a detailed dietary history, was stratified (0, 1 to 17, 18 to 34, and > or = 35 g per day). Mortality from coronary heart disease, ascertained from death certificates, was classified as death from myocardial infarction (sudden or nonsudden) or death from other coronary causes. RESULTS: During 47,153 person-years of follow-up, there were 430 deaths from coronary heart disease; 293 were due to myocardial infarctions (196 were sudden, 94 were nonsudden, and 3 were not classifiable). Cox proportional-hazards regression showed that for men who consumed 35 g or more of fish daily as compared with those who consumed none, the relative risks of death from coronary heart disease and from sudden or nonsudden myocardial infarction were 0.62 (95 percent confidence interval, 0.40 to 0.94) and 0.56 (95 percent confidence interval, 0.33 to 0.93), respectively, with a graded relation between the relative risks and the strata of fish consumption (P for trend = 0.04 and 0.02, respectively). These findings were accounted for by the relation of fish consumption to nonsudden death from myocardial infarction (relative risk, 0.33; 95 percent confidence interval, 0.12 to 0.91; P for trend= 0.007). CONCLUSIONS: These data show an inverse association between fish consumption and death from coronary heart disease, especially nonsudden death from myocardial infarction.**

MAIN MESH HEADINGS:
- **Coronary Disease/*mortality**
- ***Diet**
- ***Fishes**
- ***Meat**
- **Myocardial Infarction/*mortality**

ADDITIONAL MESH HEADINGS:
- **Adult**
- **Animal**
- **Coronary Disease/prevention & control**
- **Death, Sudden, Cardiac/epidemiology**
- **Follow-Up Studies**
- **Human**
- **Male**
- **Middle Age**
- **Multivariate Analysis**
- **Myocardial Infarction/prevention & control**
- **Proportional Hazards Models**
- **Risk**
- **Support, Non-U.S. Gov't**
- **Support, U.S. Gov't, P.H.S.**

PUBLICATION TYPES: **JOURNAL ARTICLE**

LANGUAGES: Eng
GRANT/CONTRACT ID: HL 03387/HL/NHLBI
HL 15174/HL/NHLBI
HL 21010/HL/NHLBI

Related Articles

TITLE: Fish consumption and cardiovascular disease in the physicians' health study: a prospective study.

AUTHORS: Morris MC; Manson JE; Rosner B; Buring JE; Willett WC; Hennekens CH

AUTHOR AFFILIATION: Department of Epidemiology, Harvard School of Public Health, Boston, MA, USA.

SOURCE: Am J Epidemiol 1995 Jul 15;142(2):166-75

CITATION IDS: PMID: 7598116 UI: 95321324

ABSTRACT: The authors examined the association between dietary intake of fish and omega 3 fatty acids from seafood and the risk of cardiovascular disease in a prospective cohort study of 21,185 US male physicians who are participants in the Physicians' Health Study. In 4 years of follow-up, there were 281 incident cases of total (fatal and nonfatal) myocardial infarction, 173 cases of stroke, and 121 cardiovascular deaths. There was no evidence for association between dietary intake of fish and any cardiovascular endpoint, including myocardial infarction, stroke, and cardiovascular death. The relative risks of total myocardial infarction, adjusted for age and randomized treatment assignment, for categories of fish intake were: 1.0 for < 1 meal/week (referent), 1.6 (95% confidence interval (Cl) 1.1-2.3) for 1 fish meal/week; 1.4 (95% Cl 1.0-2.0) for 2-4 fish meals/week; and 1.2 (95% Cl 0.6-2.2) for > or = 5 fish meals/week; chi 2 for trend = 0.9, p = 0.34. The relative risks were similar for omega 3 fatty acid intake and for specific types of fish, and did not change after adjustment for history of hypertension, hypercholesterolemia, diabetes mellitus, or angina pectoris, parental history of myocardial infarction before age 60 years, obesity, exercise, smoking, alcohol use, saturated fat intake, and vitamin supplement use. These data do not support the hypothesis that moderate fish consumption lowers the risk of cardiovascular disease.

MAIN MESH HEADINGS:
Cardiovascular Diseases/*epidemiology
*Diet
*Fatty Acids, Omega-3
*Seafood

ADDITIONAL MESH HEADINGS:
Aged
Cerebrovascular Disorders/epidemiology
Follow-Up Studies
Health Surveys
Human
Male
Middle Age
Multivariate Analysis

	Myocardial Infarction/epidemiology **Proportional Hazards Models** **Prospective Studies** **Risk Factors** **Support, U.S. Gov't, P.H.S.**
PUBLICATION TYPES:	**JOURNAL ARTICLE**
CAS REGISTRY NUMBERS:	**0 (Fatty Acids, Omega-3)**
LANGUAGES:	**Eng**
GRANT/CONTRACT ID:	**HL-26490/HL/NHLBI** **HL-34595/HL/NHLBI** **CA-34944/CA/NCI** +

Related Articles

TITLE:	**Fish consumption and sudden cardiac death [editorial; comment]**
AUTHORS:	**Kromhout D**
SOURCE:	**JAMA 1998 Jan 7;279(1):65-6**
CITATION IDS:	**PMID: 9424048 UI: 98084664**
COMMENT:	**Comment on: JAMA 1998 Jan 7;279(1):23-8**
MAIN MESH HEADINGS:	**Death, Sudden, Cardiac/*epidemiology** ***Seafood**
ADDITIONAL MESH HEADINGS:	**Diet** **Human** **Risk**
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